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痰热清治疗对 AECOPD 患者症状、血气、肺功能指标及炎症因子水平的影响*

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摘要 目的:探究痰热清对慢性阻塞性肺疾病发作加重期(AECOPD)患者的症状、血气、肺功能指标及炎症反应的影响。**方法:**选择 2017 年 10 月至 2018 年 10 月在本医院就诊的 AECOPD 患者共 100 例,将其随机分为 A 组(对照组)和 B 组(研究组),每组各 50 例。A 组进行常规治疗,B 组在 A 组治疗方案的基础上给予痰热清治疗,比较两组患者的治疗效果、治疗前后血气指标、肺功能及血清炎症因子水平的变化。**结果:**治疗后,B 组咳嗽、呼吸困难和啰音消失时间显著性短于 A 组($P<0.05$);两组血氧饱和度(SpO_2)均较治疗前显著上升($P<0.05$),动脉血二氧化碳分压($PaCO_2$)、血清白细胞介素-1(IL-1)、C 反应蛋白(CRP)和降钙素(PCT)水平均较治疗前显著降低($P<0.05$),且 B 组 SpO_2 显著高于 A 组($P<0.05$), $PaCO_2$ 及血清 IL-1、CRP 及 PCT 水平均显著低于 A 组($P<0.05$)。**结论:**痰热清辅助常规治疗可显著改善 AECOPD 患者临床症状,有效改善肺功能,减轻炎症反应。

关键词:痰热清;慢性阻塞性肺疾病发作加重期;肺功能;炎症因子

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Effects of Phlegmyheatclear Treatment on the Symptoms, Blood gas, Lung Function and serum Inflammatory Factors Levels of AECOPD Patients*

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ABSTRACT Objective: To explore the effect of phlegmyheatclear on the symptoms, blood gas, lung function and inflammatory response in patients with exacerbation of chronic obstructive pulmonary disease (AECOPD). **Methods:** 100 patients with AECOPD who were treated in our hospital from October 2017 to October 2018 were selected and randomly divided into group A (control group) and group B (study group), with 50 cases in each group. Group A was treated with conventional therapy, while group B was treated with phlegmyheatclear on the basis of treatment plan of group A, the therapeutic effect, changes of blood gas index, lung function and serum inflammatory factors before and after treatment were compared between two groups. **Results:** After treatment, the coughing, dyspnea and rale disappearance time of group B were significantly shorter than those of group A ($P<0.05$). The blood oxygen saturation of both groups (SpO_2) were significantly increased after treatment ($P<0.05$), and the levels of arterial carbon dioxide partial pressure ($PaCO_2$), serum interleukin-1 (il-1), c-reactive protein (CRP) and calcitonin (PCT) were significantly decreased ($P<0.05$), the SpO_2 levels in group B were significantly higher than those of group A ($P<0.05$), and the levels of $PaCO_2$ and serum IL-1, CRP and PCT were significantly lower than those of group A ($P<0.05$). **Conclusion:** Phlegmyheatclear can significantly improve the clinical symptoms of AECOPD patients, it can effectively improve the lung function, reduce the inflammatory response.

Key words: Phlegmyheatclear; Exacerbating phase of copd; Pulmonary function; Inflammatory factors

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前言

慢性阻塞性肺病(COPD)的特征是持续性的呼吸道症状^[1]。据统计,全世界慢性阻塞性肺病病例超过 3 亿,每年约有 300 万人因此病而死亡^[2],中国有 9990 万成人患有慢性阻塞性肺病,并且慢性阻塞性肺病急性加重(AECOPD)的患者越来越多^[3]。AECOPD 是指 COPD 患者呼吸系统症状的急性加重,该病通常与气道炎症和粘液生成增加以及明显的气体滞留有关,是 COPD 患者预后的主要决定因素,通常以传统治疗方法或辅

助中药祛痰为主^[4,5]。痰热清注射液是国家二类新药,由黄芩、熊胆粉、山羊角、金银花、连翘五味中药组成,主要用于肺炎早期、急性支气管炎、慢性支气管炎急性发作以及上呼吸道感染证属风温肺热病,同时具有抗炎和杀菌灭毒等作用,能显著性提高患者免疫功能。因此,本研究探讨了在传统治疗方法的基础上辅助痰热清治疗 AECOPD 患者的临床效果及对患者症状、血气、肺功能指标及炎症因子水平的影响,从而为痰热清大肆推广使用奠定一定的基础。

1 材料与方法

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1.1 临床资料

选择 2017 年 10 月至 2018 年 10 月在本院就诊, 年龄在 36-78 岁的 AECOPD 患者共 100 例, 将随机分为 A 组(对照组)和 B 组(研究组), 每组各 50 例。其中, A 组(男 27 例, 女 23 例)平均年龄 49.73 ± 7.92 岁, B 组(男 26 例, 女 24 例)平均年龄 49.12 ± 7.67 岁, 两组患者年龄($P>0.05$), 性别($P>0.05$), 身体质量指数($P>0.05$), 家族病史($P>0.05$), 吸烟史($P>0.05$), 糖尿病史($P>0.05$), 高血压病史($P>0.05$), APPACHE II 等比较均无统计学差异, 具有可比性。两组患者符合 AECOPD 诊断标准, 排除标准: 1) 有中草药过敏禁忌证患者, 2) 精神异常者和重大疾病者, 3) 暴躁不服从医务人员者。两组患者均自愿参与本研究, 已签署知情同意书, 且该研究通过了本院伦理。

1.2 治疗方法

根据患者的病情进行药物治疗和常规处理及管理。A 组给予吸氧、注射用多索茶碱解痉、吸入糖皮质激素抗炎、注射用头孢哌酮舒巴坦抗感染、纠正电解质和酸碱失衡等常规治疗, 连续治疗 7 d。B 组在 A 组的基础上给予痰热清注射液(痰热清注射液由上海凯宝药业公司生产, 规格 10 mL/支, 生产批号: 1204369、130516), 用法为 20 mL 加入到 250 mL 0.9% 氯化钠注射液中, 1 次/d 静滴。

1.3 评价指标

1) 症状: 随时监测两组患者生命体征, 根据 COPD 疗效评

定标准^[6]进行评定咳嗽、气促和哮鸣音等临床症状消失或转归的时间, 比较两组患者治疗效果。

2) 血气分析指标: 采用雅培血气分析仪测定两组研究对象接受治疗前 1 d 和接受治疗后 5 d 血氧饱和度(SpO_2)、动脉血二氧化碳分压(PaCO_2)等变化。

3) 肺功能监测: 采用肺功能仪监测两组研究对象治疗前 1 d 和接受治疗后 1 d 肺功能各项指标的变化, 包括一秒钟用力呼气容积(FEV1)和呼气流量峰值(PEF)变化等。

4) 炎症因子检测: 抽取两组研究对象治疗前 1 d 和接受治疗后 1 d 的空腹外周血 3 mL, 离心取上清, 采用 ELISA 技术检测炎症因子白细胞介素-1(IL-1)、C 反应蛋白(CRP)和降钙素(PCT)。

1.4 统计学方法

采用 SPSS 19.0 版统计学软件对本试验数据进行分析, 计数资料以(n)或(%)表示, 组间比较采用 χ^2 检验; 计量资料以(mean $\pm$ SEM)表示, 组间比较采用 t 检验。以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

如表 1 所示, B 组患者咳嗽、呼吸困难和啰音消失时间均显著性比 A 组显著缩短($P<0.05$)。

表 1 两组咳嗽、呼吸困难和啰音消失时间的比较($\bar{d}, \bar{x} \pm s$)

Table 1 Comparison of the disappearance time of cough, dyspnea and rale between group A and group B ($\bar{d}, \bar{x} \pm s$)

Groups	n	Cough	Dyspnea	Pulmonary rales disappear
Group A	50	5.47 ± 1.21	5.34 ± 1.72	4.93 ± 0.91
Group B	50	4.89 ± 1.45	3.68 ± 1.09	3.11 ± 0.78
t		2.172	5.764	11.033
P		<0.05	<0.05	<0.05

2.2 两组治疗前后血气指标的比较

如表 2 所示, A、B 两组治疗后的血氧饱和度(SpO_2)均较治疗前显著上升($P<0.05$), 而动脉血二氧化碳分压(PaCO_2)均较治

疗前显著性降低 ($P<0.05$), 且 B 组 SpO_2 明显高于 A 组($P<0.05$), PaCO_2 显著低于 A 组($P<0.05$)。

表 2 两组治疗前后血气指标的比较($\bar{x} \pm s$)

Table 2 Comparison of the blood gas indexes before and after treatment between groups A and B ($\bar{x} \pm s$)

Groups	n	$\text{SpO}_2(\%)$		$\text{PaCO}_2(\text{mmHg})$	
		Prior treatment	Posttreatment	Prior treatment	Posttreatment
Group A	50	92.02 ± 9.12	$98.11 \pm 10.27^*$	58.39 ± 4.12	$47.83 \pm 2.78^*$
Group B	50	92.34 ± 9.27	99.37 ± 10.98	58.56 ± 4.07	41.56 ± 2.07
t		-0.019	-0.056	-0.051	3.374
P		>0.05	>0.05	>0.05	<0.05

Note: Compared with before treatment, $*P<0.05$.

2.3 两组治疗前后肺功能指标的比较

如表 3 所示, 两组治疗前 FEV₁ 和 PEF 比较无显著差异($P>0.05$), 两组治疗后 FEV₁ 和 PEF 均较治疗前显著升高($P<0.05$), 且 B 组以上指标显著高于 A 组($P<0.05$)。

2.4 两组治疗前后血清炎症因子水平的比较

如表 4 所示, 两组治疗前血清白细胞介素-1(IL-1)、C 反应蛋白(CRP)和降钙素(PCT)水平比较无显著性差异, 治疗后以上指标水平均较治疗前显著降低, 且 B 组以上指标水平均显著低于 A 组。

表 3 两组治疗前后肺功能指标的比较($\bar{x} \pm s$)Table 3 Comparison of the lung function indicators before and after treatment between groups A and B ($\bar{x} \pm s$)

Groups	n	FEV ₁ (L)		PEF(L/s)	
		Prior treatment	Posttreatment	Prior treatment	Posttreatment
Group A	50	1.32± 0.17	1.87± 0.33*	1.79± 0.42	2.61± 0.37*
Group B	50	1.29± 0.23	2.27± 0.57	1.86± 0.27	3.16± 0.41
t		1.051	-9.221	-2.811	-18.033
P		>0.05	<0.05	>0.05	<0.05

Note: Compared with before treatment, * $P < 0.05$.

表 4 两组治疗前后血清炎症因子水平的比较($\bar{x} \pm s$)Table 4 Comparison of the serum inflammatory factors before and after treatment between groups A and B ($\bar{x} \pm s$)

Groups	n	TNF- α (pg/mL)		PCT(ng·L ⁻¹)		CRP(mg·L ⁻¹)	
		Prior treatment	Posttreatment	Prior treatment	Posttreatment	Prior treatment	Posttreatment
A Group	50	51.12± 3.27	38.17± 3.3*7	14.79± 6.42	4.61± 0.57*	54.79± 5.62	16.61± 1.57*
B Group	50	51.29± 3.43	32.57± 3.17	14.86± 6.27	1.16± 1.41	54.86± 5.87	14.36± 2.11
t		-0.076	2.612	-0.009	14.916	-0.011	3.253
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Note: Compared with before treatment, * $P < 0.05$.

3 讨论

慢性阻塞性肺病(COPD)常伴有急性加重(AECOPD),其占 COPD 住院患者的一半以上,是患者临床恶化和医疗费用增加的主要原因^[7],也是 COPD 患者死亡的主要原因^[10-13]。在全球,超过 50%治疗 COPD 的相关费用是由患 AECOPD 引起的,有效控制慢性阻塞性肺病慢性炎症是减少 AECOPD 的关键^[8,9]。本研究中,AEPOCE 患者在常规治疗的基础上辅助使用痰热清后咳嗽、呼吸困难和啰音消失的时间均显著性短于常规治疗,与既往研究结果相似^[16,17],可能与使用痰热清后提高了患者的免疫力的同时促进了机体对药物的吸收,从而提高了药效,增强了治疗效果等有关。

痰热清主要成分包含黄芩苷、熊胆粉、金银花、山羊角、连翘酚等中草药,不仅具有抗病毒、抗应激、解痉、镇痛、祛痰、平喘、抗菌、抗炎等作用,同时具有清热解暑和抗流感能力,可提高非特异性免疫功能^[14,15]。COPD 患者可能是因为气道炎症因子升高导致内皮功能障碍,而内皮损伤与支气管梗阻的严重是导致 AOPECD 病因形成的主要原因。本研究 AOPECD 患者在常规治疗的基础上辅助痰热清治疗,患者治愈率显著性提高的同时肺功能明显改善,这可能与痰热清不仅具有改善人体免疫的功能,同时痰热清具有清热解毒和抗流感的作用,遏制了内皮损伤等有关。此外,痰热清主要作用于肺微循环中,在维持内皮态中发挥重要作用等有关^[18,19],因此在辅助治疗 AECOPD 中具有显著效果。

由于目前监测手段的敏感性和可靠性较差,使用 SpO₂ 监测 AECOPD 患者治愈水平一直存在争议^[20-22]。目前,虽然 GOLD 并不推荐在 AECOPD 期间测量 SpO₂ 来表示肺功能变化,但是在没有 MICD 的情况下,SpO₂ 被广泛用于表示血气指标,提示 AECOPD 恢复情况^[23,24]。本研究中,AECOPD 患者使用

痰热清后一秒钟用力呼气容积(FEV₁)和呼气流量峰值(PEF)均显著性高于接受常规治疗的 AECOPD 患者,该结果与既往研究结果相似^[25,26],这可能与辅助痰热清治疗可有效减轻呼吸道炎症和水肿、缓解痉挛、改善呼吸功能、增加血氧饱和度、降低 PaCO₂、等有关。

炎症是 COPD 发展的重要因素,本研究结果显示使用痰热清组的 AECOPD 患者血清 IL-1、CRP 和 PCT 水平均显著低于接受常规治疗的 AECOPD 患者。既往研究显示痰热清具有明显的抗炎平喘的作用,可减轻呼吸系统炎症的作用,抑制 TLRs 相关通路。因此,痰热清中的活性物质可通过抑制相关通路中的部分蛋白的表达,同时抑制 NLRP3 的表达,从而下调 IL-1 等水平的降低,减少炎症反应,提高临床 AECOPD 的临床效果^[27-31]。

综上所述,痰热清辅助常规治疗可显著改善 AECOPD 患者临床症状,有效改善肺功能,减轻炎症反应。

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